

SUBDERMAL CONTRACEPTIVE IMPLANT

I. INTRODUCTION

The subdermal contraceptive implant (IMPLANON®/NEXPLANON®) is a long-acting, reversible, hormonal contraceptive that contains 68 mg etonogestrel (progesterone-only) and is effective for up to 3 years. The implant is a sterile, latex-free single-rod 4 cm in length and 2 mm wide. The rod initially releases between 60-70 mcg etonogestrel per day but declines slowly over time (etonogestrel blood levels inhibit ovulation for at least three years in most women).

The primary mechanisms of action of the subdermal contraceptive implant include suppression of ovulation, increased viscosity of cervical mucus and alterations in the endometrium.

In 2010 Implanon® was replaced by Nexplanon®. The hormone type and dose have not changed and the only difference in the implant itself was the addition of barium sulfate to allow x-ray location of the implant (Implanon® was not radio-opaque, making it difficult to locate when there was a question about implant location). The only other difference between the two products is the inserter.

In order to provide this contraceptive method, providers must undergo training for insertion and removal by a manufacturer-approved trainer.

In 2016, reports of migration of the implant within the arm from the insertion site (which may be related to deep insertion), as well as post-marketing reports of implants located within the vessels of the arm and the pulmonary artery (which may be related to deep insertions or intravascular insertion) resulted in updated insertion guidance. Angle of insertion was amended to an angle of less than 30°, with avoidance of insertion over the sulcus (groove) between the biceps and triceps and the large blood vessels and nerves that lie there in the neurovascular bundle deeper in the subcutaneous tissue. It must be kept in mind that significant migration of contraceptive implants is rare, especially when proper insertion techniques are utilized. Migration into the chest wall or vasculature is extremely rare - the reporting rate of migration into the vasculature is about 1.3 per million implants sold.

II. CLIENT SELECTION

A. Indications: Contraceptive implants and intrauterine devices (IUD) are top-tier contraceptive options and **should be highly encouraged for all women, especially adolescents**.

1. Implants and IUDs have lower failure (pregnancy) rates, higher continuation rates and improved safety when compared with other reversible hormonal or non-hormonal methods of contraception.
2. Of note, USMEC July 2016 update NO LONGER restricts use of the contraceptive implant in the following conditions (USMEC 1 No restriction [method can be used]):
 - a. Rheumatoid Arthritis-Immunosuppressive therapy – (USMEC 1, prior USMEC 3 for continuation)

b. Migraine with aura at any age (USMEC 1, prior USMEC 3 for continuation)

B. Contraindications (USMEC 3-- Risks outweigh advantages for method use; USMEC 4-- Unacceptable risk for method use):

1. Breast Cancer – (current USMEC 4)
2. Unexplained vaginal bleeding (USMEC 3 before evaluation)
3. Breast cancer (Current: USMEC 4. Past: no evidence of disease for > 5 years: USMEC 3)
4. History of myocardial infarction, ischemic heart disease or stroke (USMEC 3)
5. Cirrhosis (severe-decompensated) (USMEC 3)
6. Liver tumors – benign hepatocellular adenoma or malignant hepatoma (USMEC 3)
7. Systemic Lupus Erythematosus –positive (or unknown) antiphospholipid antibodies (USMEC 3)

C. Drug interactions

There is limited direct evidence regarding potential drug interactions between the subdermal implants (etonogestrel) and various medications, which might result in alterations in drug levels (typically a reduction in etonogestrel), which could increase failure of the subdermal implant.

1. Certain liver-enzyme inducing medications, including certain antiretroviral medications (ARV)
2. Certain antiepileptic medications (AED),
3. Rifampicin/rifabutin,

For these patients, the subdermal implant is not contraindicated (USMEC 2 or 1). However, these patients should be encouraged to use dual-method contraception (condoms with the subdermal implant) in order to decrease risk of contraceptive failure. They should also be encouraged to notify their other health care providers of all contraceptives being used.

III. MEDICAL SCREENING AND EVALUATION

- A. An appropriate (targeted) history, height, weight, blood pressure measurement and laboratory testing as indicated should be completed prior to the provision of subdermal contraceptive implant.
- B. Patients should be encouraged to receive routine health maintenance, including annual examination. However, initiation or use of contraception should not be delayed or withheld due to a need for routine health maintenance.
- C. Written results of a physical exam done elsewhere within the last 12 months are acceptable (with the exception of history, height, weight and blood pressure - which must be taken and documented prior to providing implant).
- D. Pelvic exams are not required until age 21 years unless indicated (ACOG).
 1. Pelvic examinations are not required prior to initiation of a subdermal implant for any patient.
 2. Pelvic examinations should only be performed if needed as a part of preventative services (eg: annual exam) or if the patient has a medical complaint requiring evaluation.
 3. There is no time at which a pelvic exam is required for initiation or continued provision of the method as long as all eligibility requirements are met.
- E. Pap test screening according to current screening recommendations and site- approved protocols should be followed. Initiation of a subdermal implant method, should not be

delayed or withheld for patients who have not completed recommended screening, including pap smear or STI testing.

IV. WOMEN WITH SPECIAL CONDITIONS REQUIRING FURTHER EVALUATION

- A. Decisions regarding individualized management, follow-up intervals, and the need for additional testing or referral must be made based on protocols approved by the site Medical Director. In addition, there should be consultation with the site Medical Director as needed.
- B. Consultation may be appropriate to discuss possible use of a subdermal implant in women with comorbid conditions resulting in a USMEC 3 rating. For some of these patients, use of the subdermal implant may be appropriate.
- C. Data has not shown a significant change in effectiveness in overweight or obese women.
 - Use of the subdermal implant in overweight / obese women is USMEC Cat 1.

V. CLIENT EDUCATION/ INFORMED CONSENT

All clients being provided a subdermal contraceptive implant should receive the following:

- A. Information/counseling regarding all contraceptive options available
- B. Information specific to hormonal contraceptive method of choice including effectiveness, benefits, risks, use, danger signs, potential side effects, complications and discontinuation issues.
- C. Information that implant does not offer protection against STIs/HIV. The routine use of condoms should be encouraged to decrease STI risk.
- D. Informed consent (form attached to this guideline) should be reviewed and signed and a copy of the same, upon request.
- E. If implant is being provided/prescribed to a client with risk factors, then a Request for Contraception in Women with Risk Factors form should be reviewed and signed.
- F. A copy of the FDA approved Patient Package Insert (PPI).
- G. User card in the implant kit (write in insertion date, lot #, removal date).
- H. Instruction/counseling on importance of reading the Patient Package Insert (PPI).
- I. Emergency, 24-hour telephone number and location where emergency services can be obtained.
- J. Clinic access information.

VI. SUBDERMAL CONTRACEPTIVE IMPLANT INITIATION

- A. Follow manufacturers updated instructions for insertion.
- B. Pregnancy must be excluded before insertion.
- C. Emergency procedure must be in place to manage vaso-vagal fainting episodes.
- D. Timing of Initiation - the table below should be followed when initiating the contraceptive implant. Alternative timings must be individualized to ensure contraceptive protection.

Current Method	IMPLANON®/NEXPLANON® Insertion	Back-Up
None (in the past month)	Days 1 thru 5 of the menstrual cycle	If more than 5 days since menstrual bleeding started but prior to ovulation and pregnancy test negative, use backup for 7 days

		<p>after insertion.</p> <p>If patient is in luteal phase (post-ovulation) and has had unprotected intercourse, even with a negative pregnancy test at that visit, the patient should use condoms or abstain from intercourse for two weeks, then return for a repeat pregnancy test. If that repeat pregnancy test is negative, then the implant may be inserted.</p>
<p>Combination Hormonal Contraceptive</p> <p>a. COC</p> <p>b. Ring</p> <p>c. Patch</p> <p>Progestin Only Pill</p> <p>d. POP</p>	<p>Can insert anytime in cycle if pregnancy can reliably be ruled out</p> <p>OR</p> <p>a. Anytime within 7 days of the last active COC pill</p> <p>b. Anytime during the 7 day ring-free period</p> <p>c. Anytime during the 7 day patch-free period</p> <p>d. Any day of the month (do not skip any days between the last POP pill and insertion of IMPLANON®/NEXPLANON®)</p>	None
IMPLANON®/NEXPLANON®	On same day implant is removed	None
DMPA	On the day the next injection is due	None
IUCs	<p>Any time in cycle (assure not pregnant)</p> <p>Within first 5 days of menses (remove IUC same day)</p> <p>Beyond first 5 days of menses (admits to sexual intercourse this cycle)---Delay removal of IUC until next menses</p> <p>Beyond first 5 days of menses (admits to no sexual intercourse this cycle)</p>	<p>None</p> <p>Delay removal of IUC until next menses</p> <p>Back-up for 7 days after insertion</p>
1st trimester abortion or miscarriage	<p>a. Within first 5 days following a complete first trimester abortion</p> <p>b. If beyond 5 days following complete first trimester abortion, follow instructions for “No hormonal contraceptive use in past month”</p>	None
Post partum or 2 nd trimester abortion	<p>a. Between 21-28 days post-partum (if not exclusively breast feeding)</p> <p>b. Between 21-28 days following 2nd</p>	<p>None</p> <p>Back-up for 7 days after insertion</p>

	<p>trimester abortion (no intercourse)</p> <p>c. If >4 weeks post-partum (and exclusively breastfeeding) verify that client is not pregnant</p>	Back-up for 7 days after insertion with non-hormonal method
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VII. MANAGEMENT OF SIDE-EFFECTS AND COMPLICATIONS

A. Irregular Bleeding Patterns:

1. Clients are likely to have changes in their vaginal bleeding patterns, including unpredictable changes in bleeding frequency or duration, or even amenorrhea. On average, patients report 17.7 days of bleeding or spotting every 90 days. Pre-emptive education that irregular bleeding/spotting is expected, and reassurance counseling should be provided as well as parameters of what would be considered bleeding that is outside of what is expected with an implant.
2. Obtain/perform the following:
 - a. Interval history with focus on the possibility of pregnancy or genital tract infection.
 - b. Pelvic examination, as indicated, to exclude pregnancy, infection, or an anatomic lesion.
 - c. Laboratory tests:
 - i. Highly sensitive pregnancy test, if indicated. Test may need to be repeated in two weeks if initial test is negative and a very early pregnancy is suspected.
 - ii. Hemoglobin, if history suggests prolonged or heavy bleeding. If **<10**, refer for medical evaluation.
 - iii. Gonorrhea and Chlamydia tests and/or wet mount, if a vaginal, cervical or upper tract infection is suspected.
3. If inter-menstrual bleeding becomes problematic, the client may try over the counter (OTC) medication such as Ibuprofen 800 mg PO TID for 5 days.
4. Instruct the client that treatment may temporarily improve bleeding pattern, but there is substantial possibility that the irregular pattern will return after discontinuation of treatment.
5. Discontinuation may be required if the client continues to find the bleeding intolerable.

B. Possible Pregnancy:

1. In the rare event of a failure of the contraceptive device, there may be an increased risk of ectopic pregnancy.
2. Obtain/perform the following:
 - a. Interim history update, focusing on pregnancy signs and symptoms.
 - b. Pelvic examination, as indicated, to evaluate uterine softening or enlargement, adnexal tenderness or mass.
 - c. Highly sensitive urine pregnancy test.
 - i. If positive, evaluate for symptoms and signs of ectopic pregnancy; begin workup or refer immediately if suspected.

C. Headache:

1. In clinical trials, 24.9% of IMPLANON® users reported headache as an adverse event.
2. Obtain a headache history in an attempt to differentiate tension headache from migraine.
3. If the headaches seem to be of the tension variety, explain that discontinuation of the subdermal implant is unlikely to change the pattern.
4. For mild headaches without neurological symptoms, attempt treatment with ibuprofen or other analgesic.

5. If analgesics fail or signs of migraine aura are present, weigh the risks and benefits of continuing the subdermal implant.
- D. Weight Change:
 1. All progestin-only methods may have a side effect of stimulating patient appetite. This effect appears to be most pronounced with DMPA, but can occur with other methods.
 - a. No progestin-containing contraceptive cause weight gain.
 - i. Changes in patient behavior (increased caloric intake) may result in weight gain.
 2. In clinical trials of the subdermal implant, 6.4% gained weight with an average of 2.8 pounds after 1 year and 3.7 pounds after 2 years.
 3. Patients may avoid or limit weight changes through monitoring and/or modification of their diet and activity.
 4. If these measures fail and weight gain becomes problematic, discontinuing implant may be useful.
- E. Carbohydrate and Lipid Metabolic Effects: implant may induce mild insulin resistance and small changes in glucose concentrations. Women with diabetes or impaired glucose tolerance must be observed by the provider managing the diabetes.
 - a. Subdermal implant use is appropriate for women with hyperlipidemias (USMEC Cat 2) and diabetes (USMEC Cat 1/2).
- F. Liver Function: If jaundice develops implant removal is recommended as the hormone in IMPLANON®/NEXPLANON® may be poorly metabolized in clients with impaired liver function.
- G. Depression: Clients with a history of depression should be monitored. It is uncommon for progestin-containing contraceptives to have a significant impact on mood; however, in rare circumstances, patients may require removal of a subdermal implant for this reason.
- H. Contact Lens Users: Clients who develop visual changes or changes in lens tolerance should be referred to an ophthalmologist for assessment.
- I. Non-palpable implant:
 1. If the implant is not palpable immediately after presumed placement, confirm its presence in the arm with 2-dimensional x-ray (for Nexplanon only)
 2. If an implant is non palpable at a later date:
 3. Evaluate for potential pregnancy
 4. Evaluate bleeding pattern indicates progestin effect or not
 5. Refer for evaluation of serum etonogestrel level and imaging for localization

VIII. FOLLOW-UP

- A. Post-insertion site check is not indicated unless the client has signs of infection at the site (red, inflamed, discharge) or other implant related complications.
- B. Advise client to report any of the following:
 1. Unable to palpate rod
 2. Heavy vaginal bleeding (lasting 14 days or longer)
 3. Delayed menses after a long interval of regular cycles
 4. Concern about possible pregnancy
 5. Arm pain, redness, bleeding/discharge at the insertion site
 6. Onset/worsening of migraine, aura, or severe headache
 7. Desire for removal
- C. Annual exams are to be scheduled by the client.
- D. Removal:

1. Implant should be removed when method change desired, pregnancy desired or implant has reached expiration date (3 years from insertion).
2. Removal should be conducted only by clinicians who have completed the manufacturer-approved implant insertion and removal training.
3. Follow removal guidelines in the manufacturer's package insert
4. Removal consent is needed.
5. Counsel the client as indicated on alternate contraceptive methods or provide preconception health information if pregnancy is desired.
6. If client desires another implant, insertion may occur immediately upon removal of the current implant.
7. Implant removal should not be attempted if implant is not palpable.
8. If implant not palpable
 - a. Rule out pregnancy,
 - b. Advise patient of need for back up method until presence of implant can be confirmed,
 - c. Refer to the manufacturers comprehensive instructions on localization that are provided during the FDA mandated placement and removal training which includes referral for localization and removal by professional familiar with anatomy of arm.

IX. DOCUMENTATION

- A. Order must be written in medical record
- B. Document on the medical record and the client's user card:
 1. Date of the insertion
 2. Type and amount of topical anesthetic
 3. 3 year removal date
 4. Location (left or right arm)
 5. Client identification (ID) number
 6. Client and provider palpated inserted rod
 7. Lot number
 8. Expiration date of implant
 9. Full Name of inserter
- C. Removal Documentation
 1. Reason for removal
 2. Type and amount of topical anesthetic
 3. Length of incision
 4. Length of time to remove
 5. Any problems encountered
 6. Site care instructions provided
 7. Full Name or remover
- D. All education/counseling must be documented

REFERENCES

CDC Medical Eligibility Criteria for Contraceptive Use. MMWR / Vol. 65 / No. 3 / July 29, 2016

Manufacturers FDA approved Patient Package Insert (PPI)